



Welcome to the Summer 2020 issue of MEDICAMENT, the Consortium for Medical Marijuana Clinical Outcomes Research's quarterly newsletter! You may read previous newsletters [here](#).

Since April 2020, the Consortium received updates from the 2019 grant cycle awardees on the progress of their research projects; reviewed new grant proposals and awarded 9 research grants for 2020; and launched a statewide survey of licensed medical marijuana providers.

With a momentous first year of activities and progress, the Consortium looks forward to new and continued research, collaborations with patients, physicians and industry partners, and the opportunity to establish the MMJ Clinical Outcomes Research Data Repository (MEMORY) to track clinical outcomes of medical marijuana use.



Consortium for Medical Marijuana Clinical Outcomes Research

To learn more about the Consortium and our programs, visit our new website at mmjoutcomes.org.

RESEARCH GRANT UPDATES

2019 RESEARCH GRANTS PROGRAM UPDATES

The 2019 recipients of the research grant funds provided their research progress reports to the Consortium at the end of May.

Despite significant setbacks faced by these researchers during the ongoing COVID-19 crisis, some were able to move ahead with their research activities as proposed and they all plan to finalize their studies by December 2020.



Efficacy of a controlled short-term trial of CBD ingestion on reducing symptomatic response and facilitating recovery after induced muscle injury

PI: Paul A. Borsa, PhD
University of Florida

Executive Summary:

Is a controlled short-term trial of CBD ingestion effective in reducing symptomatic response (e.g. musculoskeletal pain and pain-related anxiety) and facilitating functional recovery (strength loss) following induced muscle injury? Secondly, are the therapeutic effects dose-dependent? We have secured IRB approval from UF and are still in the process of obtaining an Investigational New Drug (IND) status from the Food & Drug Administration (FDA) Center for Drug Evaluation and Research (CDER). Our application is presently on clinical hold status pending additional information requested by CDER. We are in the process of securing collaboration with a Florida-based CBD company (SunFlora, Inc, St. Petersburg, FL) who has agreed to source our hemp-derived CBD for the project as well as assist in the generation of additional information requested by the FDA. We expect to obtain and IND this summer and begin data collection pending approval from the University to reinstate clinical laboratory operations.



Therapeutic dosing of a cannabinoid (CBD) after mild and moderate brain injury for translation to the clinic

PI: Helen Bramlett, PhD
University of Miami

Executive Summary:

Cannabidiol (CBD), a type of cannabinoid, has been shown to have anti-inflammatory, neuroprotective effects that may be a therapeutic strategy in the treatment of traumatic brain injury (TBI). The objective of this study is to rigorously assess two therapeutic doses (3 or 5mg/kg) of CBD using a clinically-relevant oral administration regimen in two pre-clinical models of brain injury. At this time, we have completed 50% of our preclinical injuries using either the moderate fluid percussion injury (FPI) model or blast TBI model. Animals were

orally administered 5 mg/kg CBD in peanut oil or vehicle (Veh; peanut oil alone) for 7 days after TBI or sham surgery. The FPI and Blast TBI groups have undergone their respective behavioral testing paradigms and tissue has been processed for histological analyses. The next steps will include completing the animal groups for both the Blast and FPI models with oral administration of two different concentrations of CBD. This includes conducting and analyzing neurocognitive, sensorimotor, hearing, and vestibular behavioral outcome measures, as well as histological analyses evaluating neuro- and cytoprotection and inflammatory responses. By the end of the award, with completion of proposed specific aims, we anticipate oral administration of CBD will mitigate some of the behavioral deficits and histopathological consequences resulting from FPI and Blast TBIs.



Cannabidiol: A potential treatment for migraine-like pain, negative emotion and photophobia

PI: Andrea Cippitelli, PhD
Florida Atlantic University

Executive Summary:

Based on the beneficial effects of cannabidiol (CBD), we aimed to investigate if CBD has therapeutic role in migraine pathology. Using nitroglycerin (NTG), we completed conditioned place aversion (CPA) experiments, Von Frey assay of allodynia in the paw, and grimace face assay with no significant findings. Due to multiple failed attempts and time restraints using NTG, we moved to a calcitonin gene-related peptide (CGRP) migraine model. We successfully modeled aversion in CGRP groups, however pretreatment with CBD showed no effect. The grimace face assay produced acute spontaneous pain with visible symptoms from CGRP, such as eye squinting and downward pointing of the face and we will repeat using pretreatment with CBD. A reliable method for detecting facial allodynia in the periorbital region using Von Frey filaments has proven challenging with failed attempts following acute NTG treatment and restraining/holding apparatus development difficulty, however we are now able to detect thresholds of allodynia similar to those reported in the literature. Our next steps include combination of acute CBD and CGRP treatment in all models, and well as chronic administration of CBD prior to CGRP induced migraine. Finally, we are ready to begin facial allodynia analysis, which will be measured for acute and chronic administration of CBD. By the end of the award, we are confident we will have insight into whether or not CBD may play a role in mouse models of migraine.



Characterizing community and physician-level factors associated with medical marijuana prescriber registration and patient access

PI: Joshua Brown, PharmD, PhD, MS
University of Florida

Executive Summary:

The charge of the Florida Consortium for Medical Marijuana Clinical Outcomes Research is to engage in research to evaluate the clinical outcomes of medical marijuana use in Florida residents. While one facet of these evaluations are the outcomes associated directly with use of medical marijuana products, many other factors can influence the outcomes experienced by Florida's medical marijuana patients. Thus, assessing these external factors is important to produce impactful research. Our research to date has utilized multiple extant data resources to gather, combine, refine, and map information on relevant external factors such as community health ratings, physician access, and dispensary locations. We have created interactive Tableau® based maps that provide county-level stratification of these factors to enhance understanding of their interplay. With the remaining project period, we will continue to refine these interactive maps and data visualizations, including use of a Google API, to map physician and dispensary locations with greater precision. The final product will include merging of all publicly available data sources to create a downloadable resource that can be used by other researchers. At the end of the award, we are on-track to deliver a continuously improving resource and are preparing to migrate these tools to be an open-access dashboard hosted by the Consortium and made available to the broader research community as well as the public and policymakers in Florida. Ultimately, the goal is to capture and understand the additional ecological factors that may influence an individual's access to medical cannabis as well as the outcomes they experience.

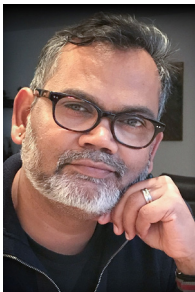


Evaluation of medical marijuana for the treatment of chronic spinal cord injury pain using a rat central neuropathic pain model

PI: Jacqueline Sagen, PhD, MBA
University of Miami

Executive Summary:

Although the most frequently reported use of medical marijuana is for pain relief, there has been a paucity of preclinical studies evaluating the effects of Cannabis components in chronic pain models. Chronic pain following spinal cord injury (SCI) occurs in a majority of patients and can be so severe that it is their top quality of life concern. Despite anecdotal observations from SCI patients reporting substantial pain relief from marijuana and medicinal extracts, progress in the field has been hampered by lack of solid supporting preclinical evidence. Thus, the goal of this study is to rigorously evaluate the effects of the two major but mechanistically distinct Cannabis components, CBD and THC, and their potential synergistic pain-relieving combination, using a preclinical SCI rodent model. Towards this goal, both male and female rats have undergone a spinal cord compression injury and tested for onset and maintenance of neuropathic pain using a battery of sensory and motor outcome measures. Results showed a gradual onset of neuropathic pain following SCI, similar to the time course observed in SCI patients. A key observation was the similarities in pain development and expression in both sexes. We have also applied for and received FDA/CSS approval for DEA Schedule 1 Researcher, but the regional field office review has been delayed due to the COVID-19 crisis. Once completed, we will test CBD/THC combinations on chronic pain reduction, dose-ranging, and daily dosing to provide the essential preclinical foundation for further guidance on medical marijuana in the treatment of chronic neuropathic pain.



A feasibility study of real-time monitoring of Posttraumatic Stress Disorder related sleep disturbances and other symptoms among patients on medical marijuana

PI: Krishna Vaddiparti, PhD, MPE, MSW
University of Florida

Executive Summary:

The goal of this pilot grant is to recruit and retain patients with Posttraumatic Stress Disorder (PTSD) on medical marijuana (MMJ) in a prospective study and examine in real-time, using Ecological Momentary Assessment (EMA) software, how MMJ affects PTSD related sleep disturbances and recovery from PTSD symptoms and distress. At this point of time there is very little scientific indication on appropriateness of marijuana as a therapy for PTSD. As of May 18th, 2020, we have 12 participants enrolled in the study and fulfilling study requirements. Most participants have been able to reach the threshold of completing 90% of the EMA surveys and have had no issues completing the REDCap surveys. Data collection is ongoing. After 20 participants have completed the study components, data will be exported from the EMA software and the REDCap database. To compare daily sleep quality, affect, PTSD symptoms, and side effects (e.g., mood, agitation) before and after starting MMJ treatment, a multilevel model will be constructed to detect changes over time for each outcome variable. We will examine the contribution of sleep disturbances to next day PTSD symptoms, after accounting for the previous evening's PTSD symptoms. To compare sleep quality, positive/negative affect, PTSD symptoms, and well-being pre and post MMJ treatment, repeated measure ANOVA will be calculated.



Marijuana-derived terpenes for the treatment of chemotherapy-induced pain

PI: Jenny L. Wilkerson, PhD
University of Florida

Executive Summary:

My current award seeks to examine cannabinoid receptor and immune mechanisms underlying the anti-allodynic and anti-depressive-like effects of terpenes and minor cannabinoids in a chemotherapy induced peripheral neuropathy (CIPN) model of neuropathic pain. I proposed to test terpenes: γ -terpinene, α -terpineol, β -caryophyllene, and the minor cannabinoids cannabichromene (CBC), cannabinol (CBN), found in marijuana in a well-characterized mouse model of CIPN. I

have two subaims for the currently funded project: Sub-aim a: Determine systemic effects of terpenes and minor cannabinoids, and mediation of effects by cannabinoid 1 receptor (CB1R), cannabinoid 2 receptor (CB2R) and Secreted

Phosphoprotein 1 (SPP1) in the CIPN model of neuropathic pain. Sub-aim b: Determine protein changes associated with mechanisms of select terpenes and minor cannabinoids in the CIPN model of neuropathic pain. Sub-aim a is complete. Sub-aim b will be completed in the months following the resumption of animal research activities at UF. The data that this grant funding has already produced are being used to submit a R21 grant next month (June 2020), with the intention of scaling up research to submit an R01 in following NIH grant cycles. Excitingly, the NIH grant proposal will leverage newly founded collaborations in pharmacokinetics and medicinal chemistry within UF. These collaborations came from presenting at the UF SPAR conference. Further, a publication with the data collected thus far is currently in preparation.



Rapid identification and quantification of heavy metals and microplastics in CBD oil.

PI: Gregory McManus, PhD
Florida Gulf Coast University

Executive Summary:

There are substantial uncertainties surrounding the nature and content of contaminants in cannabis plants. An in-depth understanding of plant contaminants and toxin effects on the stability of plant compounds and the effect on human health is necessary. The goal of this project is to develop reliable, rapid, efficient, inexpensive techniques for the determination of key contaminants within the cannabis plant and to accelerate research in this promising industry to ensure consumer/patient safety. We have begun developing and refining our methods for the testing of CBD oil samples for heavy metals and microplastics contaminants. After accomplishing the aims in this proposal, we will continue to expand the scope of our research to determine contaminants present in the marijuana vaping products using coupled Thermal Gravimetric analysis, Gas Chromatography and Mass Spectroscopy (TGA-GC-MS) techniques. For this purpose, we will seek funding through the NIH R21 program. At the conclusion of this project, we will have an understanding as to whether or not Wavelength-Dispersive X-ray Fluorescence and coupled Differential Scanning Calorimetry – Thermal Gravimetric Analysis are effective tools for identifying contaminants in CBD oil. We will have collected data on a variety of CBD oil samples and determined whether heavy metal and microplastic contaminants are present in concentrations that would pose a danger to public safety. This project will have also supported the training of two undergraduate research students during the summer of 2020.



Hyaluronic acid functionalized, Cannabidiol-loaded Mesenchymal Stem Cells (MSC)-Derived Exosomes for Drug Resistant Cancers

PI: Mandip Singh Sachdeva, PhD
Florida A&M University

Executive Summary:

Triple negative breast cancer (TNBC) represents an important clinical challenge, as these tumors often develop resistance to conventional chemotherapeutics. Anti-cancer potential of cannabidiol (CBD) is well demonstrated in various cancers but poor solubility and increased metabolism by CYP enzymes limit its bioavailability. We hypothesize that therapeutic usage of hyaluronic acid (HA) functionalized human umbilical cord stem cell derived exosomes (hUCMSCs-EX) will serve as a delivery platform not only for increasing the bioavailability but also for overcoming resistance of docetaxel (DTX) in MDA-MB-231 (i.e., CB1, CB2, and CD44 receptors expressing) cells. Synthetic CBD (Purisys™, GA; GMP grade) decreased proliferation of MDA-MB-231, MDA-MB-468 and Doxorubicin (DOX) resistant MDA-MB-231 cells. CBD could also increase sensitization of DTX and DOX to MDA-MB-231 (by 8.2 and 2.5-fold respectively) and MDA-MB-468 (by 4.6 and 3-fold respectively) cells. We also developed stable formulation of CBD loaded exosomes (CBD-EX) by using sonoporation technique. CBD-EX significantly decreased the proliferation of TNBC cells. We will further investigate the therapeutic efficacy of CBD-EX after their functionalization with HA in both wild type and drug resistant TNBC cancers. Molecular studies such as whole transcriptome analysis are currently in progress to delineate the mechanisms responsible for CBD induced-cell death. The PI expects to have stable HA-functionalized CBD-EX, which can show anti-cancer effects and enhance the sensitivity of DTX in 2D and 3D cultures of TNBC cells.



The Relationship between State Medical Marijuana Laws, Substance Use and Mental Health Disorder Diagnoses, and Associated Health Care Costs

PI: Ali M. Yurasek, PhD
University of Florida

Executive Summary:

The purpose of this project is to investigate trends regarding substance use diagnosis, mental health diagnosis, and treatment utilization in states with and without medical marijuana laws. Progress- IRB materials for the secondary data collection were submitted. The protocol received an exempt review by the University of Florida IRB and was approved. Specific activities conducted include: recruiting and training research assistants, developing a medical marijuana database (e.g., number of dispensaries, approved conditions, etc.), working with data provider, HCCI (Health Care Cost Institute), and initial identification of variables needed from NSDUH dataset. One aspect of this study (related to Aim 1) that is behind schedule is the data acquisition from the HCCI (see next section). While our request for the no cost extension is pending, a study mirroring the larger study we proposed in Aim 1 is in progress, focusing on the state of Florida. The IRB protocol is currently under review. This will allow us to obtain the relevant data, albeit on a reduced scale, and investigate one of the core hypotheses. Next Steps- 1) Finalize contract with the HCCI data provider; 2) Begin secondary data analyses with a national data set 3) finish the county level marijuana law/dispensary data for Florida and other states; and 4) Conduct GIS (Geographic Information System) analysis. Anticipated Outcomes- Findings will demonstrate the influence of MML on health care utilization for substance use and mental health diagnoses and inform health care policy and state specific medical MJ policy and implementation.

2020 RESEARCH GRANTS PROGRAM AWARDEES

In June 2020, the grants review process of the second cycle of the Consortium Research Grants program was completed.

Funding decisions were based on reviewer scores from ad-hoc out of state subject matter experts and responsiveness of the proposals to the mission and research priorities of the Consortium. Of the 20 proposed research studies, 9 were selected for funding.

The awarded research projects are from faculty belonging to 5 of the Consortium member institutions, including Florida A&M University, Florida Atlantic University, Florida State University, University of Central Florida, and University of Florida.

Funded research proposals include 6 clinical and 3 translational studies. Research outcomes and health conditions in these proposals include glioblastoma, anorexia nervosa, chemotherapy induced peripheral neuropathy, anxiety, olfactory function, food-predicting sensory cues, drug interactions, chronic pain, and pattern and motivation for medical marijuana use.



Hemp derived extracellular vesicles (EVs) for the treatment of glioblastoma

PI: Hassan Azari, PhD
University of Florida



Cannabinoid medication for treatment of a pre-clinical model of anorexia nervosa

PI: Lisa Eckel, PhD
Florida State University



Mechanisms of Action for Cannabidiol (CBD) in a Mouse Model of Anxiety

PI: Debra Fadool, PhD
Florida State University



Patterns, Motives, and Risks Associated with Marijuana Use: A Comparison of Medical Marijuana Patients and Non-Patient Marijuana Users in Florida

PI: Jason Ford, PhD
University of Central Florida



An Assessment of the Drug Interaction Potential Between Oral Cannabidiol (Epidiolex®) and the CES1 Substrate Methylphenidate in Healthy Volunteers

PI: John Markowitz, PharmD
University of Florida



Assessing and Supporting Effective and Safe Use of Medical Marijuana for Older Adults with Chronic Pain

PI: David Newman, PhD
Florida Atlantic University



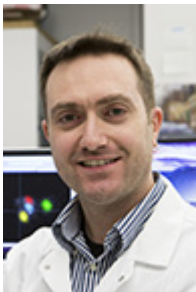
Preclinical evaluation of exosomal cannabinoid formulations in chemotherapy induced peripheral Neuropathy

PI: Mandip, Sachdeva, PhD
Florida A&M University



The influence of cannabinoid receptors on olfactory function

PI: Douglas Storace, PhD
Florida State University



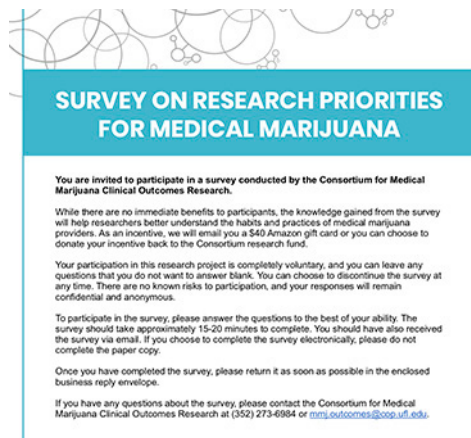
Endocannabinoid mechanism in the neural processing of food-predicting sensory cues.

PI: Roberto Vincis, PhD
Florida State University

2021 RESEARCH GRANTS PROGRAM

The Consortium will release the Request for Proposals (RFP) for the Grants Program in early 2021. You can check mmjoutcomes.org/research for updates!

PROVIDER SURVEY



SURVEY ON RESEARCH PRIORITIES FOR MEDICAL MARIJUANA

You are invited to participate in a survey conducted by the Consortium for Medical Marijuana Clinical Outcomes Research.

While there are no immediate benefits to participants, the knowledge gained from the survey will help researchers better understand the habits and practices of medical marijuana providers. As an incentive, we will email you a \$40 Amazon gift card or you can choose to donate your incentive back to the Consortium research fund.

Your participation in this research project is completely voluntary, and you can leave any questions that you do not want to answer blank. You can choose to discontinue the survey at any time. There are no known risks to participation, and your responses will remain confidential and anonymous.

To participate in the survey, please answer the questions to the best of your ability. The survey should take approximately 15-20 minutes to complete. You should have also received the survey via email. If you choose to complete the survey electronically, please do not complete the paper copy.

Once you have completed the survey, please return it as soon as possible in the enclosed business reply envelope.

If you have any questions about the survey, please contact the Consortium for Medical Marijuana Clinical Outcomes Research at (352) 273-6984 or mmj.outcomes@cop.ufl.edu.

The Consortium developed and distributed a statewide survey to more than 1600 medical marijuana providers licensed to practice in the state of Florida to help inform research priorities for the Consortium and identify training needs for providers.

If you are a physician actively certifying patients for medical marijuana in the state of Florida (within the past 12 months) and did not receive the survey, please contact us at (352) 273-6984 or mmj.outcomes@cop.ufl.edu

The Consortium is still receiving survey responses and final results will be available in the coming months. Preliminary results have been presented at the 4th annual scientific meeting of Research Society on Marijuana (RSMj) on July 24th and are available [here](#).

NEWS & EVENTS

INTRODUCING FACULTY LEAD FOR MEMORY



The Consortium welcomes Josh Brown, PharmD, PhD, MS as the Faculty Lead for MEMORY.

In 2016, Dr. Brown joined the Department of Pharmaceutical Outcomes and Policy as an assistant professor.

He has experience in clinical pharmacy, health economics and outcomes research, and pharmacoepidemiology across academic, pharmaceutical industry, and managed care. His past and ongoing clinical interests have been in the cardiovascular and hematology/oncology therapeutic areas including comparative effectiveness and safety research with a focus on anticoagulation and quality of care in thrombotic conditions such as atrial fibrillation, venous thromboembolism, and cancer.

His current research program and collaborations focus on research methods for pharmacoepidemiologic and pharmaco-economic generic and biosimilar evaluations, developing real-world evidence for drug-drug interactions, and drug repurposing studies (e.g. aging and Parkinson's Disease).

To read more about Dr. Brown, please click [here](#).

MEDICAL MARIJUANA AND COVID-19 RESEARCH AT MEMBER INSTITUTIONS

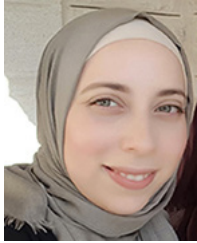
Over the last few months, researchers across the state of Florida have explored ways to address marijuana use during the COVID-19 pandemic.

Consortium member institutions are conducting research on the effects of marijuana use and coronavirus. Dr. Vidot, a marijuana researcher at the University of Miami, studies the impact that inhaling cannabis has during the pandemic. To read an article about her research, click [here](#).

RESEARCH SOCIETY ON MARIJUANA (RSMJ) CONFERENCE

The Research Society on Marijuana (RSMj) is a network of scientists with the goal to promote understanding through research of the consequences and assessment of marijuana use and the treatment of conditions including cannabis use disorder.

On July 24th, Consortium team members, Ruba Sajdeya, MD, and Sebastian Jugl, BPharm, RPh, presented posters virtually at the 4th annual scientific meeting of Research Society on Marijuana (RSMj).



Information sources and training needs on medical marijuana: preliminary results from a state-wide provider survey

Ruba Sajdeya, MD; Jennifer Jean-Jacques, MPH; Anna Shavers, MPA; Yan Wang, PhD; Nathan Pipitone, PhD; Martha Rosenthal, PhD; Almut G. Winterstein, RPh, PhD, FISPE; Robert L. Cook, MD, MPH



A mapping literature review of medical cannabis clinical outcomes and quality of evidence in approved conditions in the United States from 2016 to 2019

Sebastian Jugl, BPharm, RPh; Aimalohi Okpeku, BPharm; Brianna Costales, BS; Earl J. Morris, PharmD, MPH; Golnoosh Alipour-Harris, PharmD; Juan M. Hincapie-Castillo, PharmD, PhD; Nichole E. Stetten, PhD, MPH, CPH; Ruba Sajdeya, MD; Shailina Keshwani, BPharm; Verlin Joseph, MPH; Yahan Zhang, MS; Yun Shen, MPH; Lauren Adkins, MLIS; Amie Goodin, PhD, MPP

To view the posters, please visit the RSMj website [here](#).

CANCER EDUCATIONAL WELLNESS SERIES



As part of the UF Health Palliative Care's Cancer Educational Wellness Series, Dr. Robert L. Cook, Consortium Associate Director, presented "Medical Marijuana as a Treatment for Cancer and Cancer-Related Symptoms" on July 22nd.

During his presentation, Dr. Cook shared local research, what we have learned, and what we still have to learn about the impact medical marijuana has on cancer.

To watch the recording of Dr. Cook's presentation, click [here](#).

INTERESTED IN COLLABORATING WITH THE CONSORTIUM?

Whether you're a researcher, certifying physicians, industry partner, or a potential research participant, you can collaborate with Consortium research and activities by visiting mmjoutcomes.org/collaborate

DON'T WANT TO MISS ANY MEDICAMENT ISSUES?

To sign up for the quarterly MEDICAMENT issues from the Consortium for Medical Marijuana Clinical Outcomes Research, sign up here: mmjoutcomes.org/newsletter/